

Docket No.: 2185-0577P
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Naoyuki TAKANO et al.

Application No.: 09/971,929

Confirmation No.: 2971

Filed: October 9, 2001

Art Unit: 1654

For: PROCESS FOR PRODUCING AN AMIDE
COMPOUND

Examiner: S. R. Gudibande

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Madam:

Appellants hereby appeal the Final Rejection of August 15, 2008, issued in the above application.

A Notice of Appeal was filed February 13, 2009. Payment of the 37 CFR § 41.20(b)(2) fee for filing an Appeal Brief is submitted herewith.

I. Real Party in Interest

The real party in interest for this appeal is Nihon Medi-Physics Company, Limited of Tokyo, Japan, the assignee of record.

II. Related Appeals and Interferences

None.

III. Status of Claims

- A. There are 18 claims pending in the application.
- B. Current Status of Claims
 - 1. Claims cancelled: 6, 8, and 15
 - 2. Claims withdrawn from consideration but not cancelled: 3-5, 7, 16, and 18
 - 3. Claims pending: 1-5, 7, 9-14, and 16-21
 - 4. Claims allowed: 19
 - 5. Claims rejected: 1-2, 9-14, 17, and 20-21
- C. Claims on Appeal

The claims on appeal are claims 1-2, 9-14, 17, and 20-21.

IV. Status of Amendments

No claim amendments have been made after the Office Action dated August 15, 2008. All previous claim amendments have been entered.

V. Summary of Claimed Subject Matter

The invention on appeal is defined by independent claims 1 and 20-21 and dependent claims 2, 9-14, and 17 as described below.

The Invention of Independent Claim 1

Independent claim 1 recites a process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid (page 2, lines 5-9),

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid (page 6, line 24 to page 7, line 4); and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same (page 6, lines 3-5; page 14, lines 15-16; page 15, lines 7-13; page 16, lines 12-18; page 17, line 24 to page 18, line 4; page 18, line 24 to page 19, line 1; page 19, lines 17-19).

The Invention of Dependent Claim 2

Dependent claim 2 is directed to an embodiment wherein the compound having an amino group is a protein, a peptide, an amino acid, an amino sugar or an amine (page 2, lines 12-16).

The Invention of Dependent Claim 9

Dependent claim 9 is directed to an embodiment wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid (page 7, lines 2-4).

The Invention of Dependent Claim 10

Dependent claim 10 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid (page 6, line 24 to page 7, line 2).

The Invention of Dependent Claim 11

Dependent claim 11 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added simultaneously to the polyaminopolycarboxylic acid (page 7, lines 4-6).

The Invention of Dependent Claim 12

Dependent claim 12 is directed to an embodiment wherein the reaction is performed in the presence of a solvent (page 7, line 25 to page 8, line 1).

The Invention of Dependent Claim 13

Dependent claim 13 is directed to an embodiment wherein the solvent is at least one selected from the group consisting of water and an organic solvent (page 8, lines 2-3).

The Invention of Dependent Claim 14

Dependent claim 14 is directed to an embodiment wherein the solvent is water (page 8, lines 2-3).

The Invention of Dependent Claim 17

Dependent claim 17 is directed to an embodiment wherein the polyaminopolycarboxylic acid anhydride is ethylenediaminetetraacetic dianhydride, ethylenediaminetetraacetic acid monoanhydride, diethylenetriaminepentaacetic acid dianhydride, diethylenetriamine-pentaacetic acid monoanhydride, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic dianhydride, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid monoanhydride (page 5, lines 4-11).

The Invention of Independent Claim 20

Independent claim 20 recites a process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid (page 2, lines 5-9); wherein the polyaminopolycarboxylic acid is ethylenediamine-tetraacetic acid, diethylenetriamine-pentaacetic acid, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (page 5, line 24 to page 6, line 2),

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid (page 6, line 24 to page 7, line 4); and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same (page 6, lines 3-5; page 14, lines 15-16; page 15, lines 7-13; page 16, lines 12-18; page 17, line 24 to page 18, line 4; page 18, line 24 to page 19, line 1; page 19, lines 17-19).

The Invention of Independent Claim 21

Independent claim 21 recites a process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid and a base (page 2, lines 5-9; page 9, lines 7-8),

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid (page 6, line 24 to page 7, line 4); and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same (page 6, lines 3-5; page 14, lines 15-16; page 15, lines 7-13; page 16, lines 12-18; page 17, line 24 to page 18, line 4; page 18, line 24 to page 19, line 1; page 19, lines 17-19).

VI. Grounds of Rejection to be Reviewed on Appeal

The following Final Rejections are to be reviewed on appeal:

Claims 1, 2, 9-14, 17, and 20-21 stand finally rejected under 35 U.S.C. § 102(b) as being anticipated by **Paik et al.**, *J. Nucl. Med.*, Vol. 24, pp. 1158-1163 (1983).

Claims 1, 2, 9-14, and 21 stand finally rejected under 35 U.S.C. § 102(b) as being anticipated by **Mease et al.** '571 (US 5,021,571).

VII. Argument***A. Issues Presented for Appeal***

The issues presented for appeal are the following:

1) Have claims 1, 2, 9-14, 17, and 20-21 been anticipated in view of the disclosure of Paik et al.?

2) Have claims 1, 2, 9-14, and 21 been anticipated in view of the disclosure of Mease et al. '571?

B. Argument in Support of Patentability**1. The Present Invention and its Advantages**

The present invention is directed to a process for producing an amide compound. The amide compound is produced by reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid. The polyaminopolycarboxylic acid anhydride may be added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride may be added to the polyaminopolycarboxylic acid. In addition, the polyaminopolycarboxylic group of both the acid and the acid anhydride are the same.

This process allows the amide compound to be readily and advantageously produced through practical industrial operations in a higher yield than previously known processes. The produced amide compound is a useful intermediate for pharmaceuticals and agricultural chemicals.

2. The Legal Standard Required for Determining Anticipation

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "When a claim covers several structures or compositions, either generically or as alternatives, the claim is deemed anticipated if any of the structures or compositions within the scope of the claim is known in the prior art." *Brown v. 3M*, 265 F.3d 1349, 1351, 60 USPQ2d 1375, 1376 (Fed. Cir. 2001). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

3. ***The USPTO Fails to Show that the Prior Art Anticipates the Claims on Appeal***

Neither Paik et al. nor Mease et al. '571 disclose each and every element of Appellants' invention on appeal. As a result, claims 1-2, 9-14, 17, and 20-21 on appeal are not anticipated by the cited prior art.

a. ***The Rejection of Claims 1, 2, 9-14, 17, and 20-21 under 35 U.S.C. § 102(b) over Paik et al.***

In support of the rejection over Paik et al., the USPTO states as follows at pages 3-4 of the Final Rejection:

Paik, et al., teaches such a method of amide formation. The reference teaches the preparation of DTPA coupled serum albumin antibody. In the process, Paik, et al., affinity-purified antibody (300 µg, 2.0 nmol) was dissolved in 1 ml of 0.1M buffer solution (Hepes buffer at pH 7, phosphate at pH 7, borate at pH 8.6, or bicarbonate at pH 8.2) in a 2.5-ml vial. To the antibody solution was added solid cyclic DTPA anhydride (page 1159, column 2, paragraph 1). However, during the IR (infrared spectroscopy) analysis of the DTPA anhydride, Paik, et al., the IR spectrum showed absorption bands at 1825 and 1780 cm⁻¹, characteristic stretching vibrations for the **anhydride carbonyl group**. The IR spectrum also showed an absorption at 1640 cm⁻¹ indicating the presence of a **carboxylate group**. The claim limitation that the presence of both polyaminopolycarboxylic acid anhydride and the presence of the polyaminopolycarboxylic acid in the reaction mixture is met by the fact that the anhydride used in the preparation was a mixture of the anhydride and the free acid as shown by the IR analysis. Therefore, this meets claim limitations of claims 1 and 21. Also, during the DTPA conjugation reaction, the reaction reduced the pH of buffer solution to 4. Due to the hydrolysis of the anhydride that produced four acetic acid molecules (page 1161, column 1, paragraph 1) further affirming the presence of free polyaminocarboxylic acid in the reaction mixture. The reaction was carried out in bicarbonate buffer, pH, 8.2 as mentioned above and hence in basic condition that meets one of the limitations of claim 21 (emphasis in original).

b. ***Distinctions Between the Claimed Invention and Paik et al.***

Independent Claims 1 and 20-21

Paik et al. do not disclose each of the limitations recited in independent claims 1 and 20-21 (nor any of the claims that depend therefrom). Specifically, the independent claims recite, *inter alia*, that "the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same."

On page 4 of the Final Office Action dated August 15, 2008 and as recited above, the Examiner argues, "The claim limitation that the presence of both polyaminopolycarboxylic acid anhydride and the presence of the polyaminopolycarboxylic acid in the reaction mixture is met by the fact that the anhydride used in the preparation was a mixture of the anhydride and the free acid as shown by the IR analysis." However, the IR analysis of Paik et al. merely suggests the presence of *a carboxylate group* but not that of *a free acid molecule of the polyaminopolycarboxylic acid since it is analyzing the IR spectrum of DTPA anhydride per se as claimed*. DTPA anhydride added in the acylation reaction by Paik et al. was not a mixture of DTPA anhydride and DTPA acid.

The Examiner recites from the teachings of Paik et al. that during the DTPA conjugation reaction, the reaction reduced the pH of the (Hepes) buffer solution to 4 due to hydrolysis of the anhydride, which produced four acetic acid molecules. Although Paik et al. disclose that, after acylation reaction with DTPA anhydride, four acetic acid moieties are present per each molecule that participated in the acylation reaction, Paik et al. do not disclose nor teach the hydrolysis of DTPA anhydride to a free DTPA acid molecule.

Paik et al. also disclose the reaction of DTPA anhydride with an amino compound, carried out in bicarbonate buffer, pH 8.2, which is in a basic condition. Thus, the Examiner appears to affirm the presence of free polyaminocarboxylic acid in the reaction mixture of Paik et al. At most, Paik et al. refer to the polyaminocarboxylic acid as above but not to the polyaminopolycarboxylic acid used in the present invention.

With respect to the Examiner's reliance on Le Chatelier's Principle, Appellants respectfully assert that the Examiner's reasoning is beyond the disclosure of Paik et al.

Accordingly, the present invention is not anticipated by Paik et al. since the reference does not teach or provide for each of the limitations recited in the pending claims.

Based on the remarks above, claims 1 and 20-21 clearly distinguish over Paik et al.

Dependent Claims 2, 9-14, and 17

Dependent claim 2 is directed to an embodiment wherein the compound having an amino group is a protein, a peptide, an amino acid, an amino sugar or an amine.

Dependent claim 9 is directed to an embodiment wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid.

Dependent claim 10 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid.

Dependent claim 11 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added simultaneously to the polyaminopolycarboxylic acid.

Dependent claim 12 is directed to an embodiment wherein the reaction is performed in the presence of a solvent.

Dependent claim 13 is directed to an embodiment wherein the solvent is at least one selected from the group consisting of water and an organic solvent.

Dependent claim 14 is directed to an embodiment wherein the solvent is water.

Dependent claim 17 is directed to an embodiment wherein the polyaminopolycarboxylic acid anhydride is ethylenediaminetetraacetic dianhydride, ethylenediaminetetraacetic acid monoanhydride, diethylenetriaminepentaacetic acid dianhydride, diethylenetriamine-pentaacetic acid monoanhydride, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic dianhydride, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid monoanhydride.

Given the above-discussed deficiencies of Paik et al., the invention of claims 2, 9-14, and 17 patentably distinguishes over the disclosure of the reference.

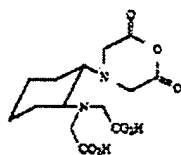
With specific respect to claims 9-11, Paik et al. clearly fail to disclose such embodiments. The cited reference discloses that the DTPA anhydride hydrolyzes in the presence of water (page 1158, column 2) with the requisite reaction occurring in the presence of polyaminopolycarboxylic acid due to the presence of hydrolyzed product of the DTPA anhydride being present in the reaction mixture. In other words, any acid which is present is due to its *in situ* formation.

Because the cited art of Paik et al. does not teach or provide for each of the limitations recited in claims 2, 9-14, and 17, the reference is not capable of supporting an anticipation rejection of any of the claims on appeal. In view of the above, the present invention is not anticipated by Paik et al.

c. **The Rejection of Claims 1, 2, 9-14, and 21 under 35 U.S.C. § 102(b) over Mease et al. '571**

In support of the rejection over Mease et al. '571, the USPTO states as follows at pages 7-8 of the Final Rejection:

Mease, et al., teaches such a method of amide formation. The reference teaches the preparation of CDTA (cyclohexyl EDTA) coupled [with] an albumin antibody (example 11, column 14). In the process, Mease, et al., prepares a conjugate of CDTA and the antibody using CDTAMA (cyclohexyl EDTA monohydrate) in the presence of 0.1 M sodium bicarbonate buffer and the CDTAMA was dissolved in DMSO (reads on instant claims 1, 2, and 12-14). The CDTAMA solution was added to the antibody solution. The CDTAMA reagent is a polyaminopolycarboxylic acid since it has two free -COOH functional groups and it is an anhydride since it has a cyclic anhydride moiety as shown in the figure below:



Both the acid and the anhydride are derived from the same polyaminopolycarboxylic acid as required by the instantly amended claims 1 and 21. Since the anhydride and acid belong to the same molecule, addition of the reagent CDTAMA in DMSO reads on the instant claims 1, 11 and 21.

Hence the cited reference of Mease, et al., anticipates the instant invention.

d. **Distinctions Between the Claimed Invention and Mease et al. '571**

Independent Claims 1 and 21

Mease et al. '571 do not disclose each of the limitations recited in independent claims 1 and 21 (nor any of the claims that depend therefrom). Specifically, the independent claims recite, *inter alia*, that "the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same."

With respect to the disclosure of a cyclic anhydride of Mease et al. '571 as recited in the August 15, 2008 Office Action, the Examiner interprets that both the acid and the anhydride are *derived from* the same polyaminopolycarboxylic acid. The depicted molecule shows that the molecule has an anhydride moiety and an acid moiety, but they are within a single molecule.

In stark contrast, the polyaminopolycarboxylic anhydride and the polyaminopolycarboxylic acid of the present invention are independent compounds and are different elements of the pending claims. The same polyaminopolycarboxyl group in the claims refers to a common molecular structure.

Accordingly, the present invention is not anticipated by Mease et al. '571 since the reference does not teach or provide for each of the limitations recited in the pending claims.

Based on the remarks above, claims 1 and 21 clearly distinguish over Mease et al. '571

Dependent Claims 2 and 9-14

Dependent claim 2 is directed to an embodiment wherein the compound having an amino group is a protein, a peptide, an amino acid, an amino sugar or an amine.

Dependent claim 9 is directed to an embodiment wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid.

Dependent claim 10 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid.

Dependent claim 11 is directed to an embodiment wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added simultaneously to the polyaminopolycarboxylic acid.

Dependent claim 12 is directed to an embodiment wherein the reaction is performed in the presence of a solvent.

Dependent claim 13 is directed to an embodiment wherein the solvent is at least one selected from the group consisting of water and an organic solvent.

Dependent claim 14 is directed to an embodiment wherein the solvent is water.

Given the above-discussed deficiencies of Mease et al. '571, the invention of claims 2 and 9-14 patentably distinguishes over the disclosure of the reference.

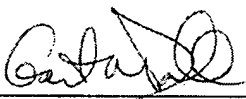
Because the cited art of Mease et al. '571 does not teach or provide for each of the limitations recited in claims 2 and 9-14, the reference is not capable of supporting an anticipation rejection of any of the claims on appeal. In view of the above, the present invention is not anticipated by Mease et al. '571.

CONCLUSION

The Final Rejection of claims 1-2, 9-14, 17, and 20-21 is improper as the USPTO fails to show that either Paik et al. or Mease et al. '571 anticipates the claims on appeal. The Final Rejection should accordingly be reversed by the Honorable Board.

Dated: April 13, 2009

Respectfully submitted,

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VIII. Claims Appendix

Claims Involved in the Appeal

1. A process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid,

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid; and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same.

2. The process according to claim 1, wherein the compound having an amino group is a protein, a peptide, an amino acid, an amino sugar or an amine.

9. The process according to claim 1, wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid.

10. The process according to claim 1, wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid.

11. The process according to claim 10, wherein the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added simultaneously to the polyaminopolycarboxylic acid.

12. The process according to claim 1, wherein the reaction is performed in the presence of a solvent.

13. The process according to claim 12, wherein the solvent is at least one selected from the group consisting of water and an organic solvent.

14. The process according to claim 13, wherein the solvent is water.

17. The process according to claim 1 or 16, wherein the polyaminopolycarboxylic acid anhydride is ethylenediaminetetraacetic dianhydride, ethylenediaminetetraacetic acid monoanhydride, diethylenetriaminepentaacetic acid dianhydride, diethylenetriaminepentaacetic acid monoanhydride, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic dianhydride, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid monoanhydride.

20. A process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid; wherein the polyaminopolycarboxylic acid is ethylenediamine-tetraacetic acid, diethylenetriamine-pentaacetic acid, or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid,

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid; and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same.

21. A process for producing an amide compound, which comprises reacting a compound having an amino group with a polyaminopolycarboxylic acid anhydride in the presence of the polyaminopolycarboxylic acid and a base,

wherein the polyaminopolycarboxylic acid anhydride is added to a mixture of the compound having an amino group and the polyaminopolycarboxylic acid, or the compound having an amino group and the polyaminopolycarboxylic acid anhydride are added to the polyaminopolycarboxylic acid; and

wherein the polyaminopolycarboxylic group of both said acid and said acid anhydride are the same.

IX. Evidence Appendix

None.

X. Related Proceedings Appendix

None.